UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,073	07/17/2007	Yves Claude Nicolau	ACI-0403 (13704.105012)	4203

20786 7590 03/24/2010

KING & SPALDING
1180 PEACHTREE STREET , NE
ATLANTA, GA 30309-3521

EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,073	NICOLAU ET AL.	
	Examiner	Art Unit	
	YUNSOO KIM	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-27* is/are pending in the application.

4a) Of the above claim(s) *21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :10/2/09, 10/26/09, 10/28/09,2/19/10.

DETAILED ACTION

1. Claims 19-27 are pending.

Claims 21 and 22 stand withdrawn from further consideration by the examiner under 37CFR 1.142(b) as being drawn to a nonelected invention.

Since a prior art revealed no prior art on SEQ ID NO:5, the search has extended to include SEQ ID NO:1.

Claims 19, 20 and 23-27 read on SEP ID NO:1 as an amyloid peptide and palmitic acid as elected species are under consideration in the instant application.

2. Applicants' submission of IDS filed on 10/2/09, 10/26/09, 10/28/09 and 2/19/10 has been acknowledged.

3. Applicant has indicated in the remark filed on 12/10/09 that the present invention is directed to methods of delaying or reducing the progression of Alzheimer's disease (p. 4). However, the title of the invention does not reflect the invention to which the claims are directed.

3. In light of Applicant's amendment filed on 12/10/09, the rejection set forth in the office action mailed on 8/11/09 (see sections 4--5) has been withdrawn.

4. The following rejections remain.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing antigenicity by administering supramolecular antigenic construct comprising an antigenic peptide with a modification, does not reasonably provide enablement for methods of delaying or reversing the progression of Alzheimer's diseases comprising administering supramolecular antigenic constructs or the use of supramolecular constructs to treat disorders comprising Alzheimer's diseases, multidrug resistance in cancer cells or prion diseases.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

The claimed is drawn to the method of delaying or reversing the progression of Alzheimer's disease comprising administering a supramolecular construct and the construct may be used in treating disorders comprising Alzheimer's disease, multidrug resistance in cancer cells or prion diseases. Wolf-Klein et al teaches that there is no medical treatment currently available to cure of stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.)

Tagliavini et al. (Journal of Virology, 2003, vol. 77, no. 15, p. 8462-8469) teach that there is no effective therapy for prion diseases including spongiform encephalopathy and Creutfeldt-Jacob diseases and some candidates are still being validated (abstract, discussion, in particular)

In addition, Applicants have not provided any *in vivo* working examples that the supramolecular constructs can be used in treatment for multidrug resistance in cancer cells or prion diseases.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's response and amendments to the claims filed on 12/10/09 have been fully considered but they were not persuasive.

Applicant has asserted that the current amendment reciting "delaying or reversing the progression of Alzheimer's disease" obviates the rejection.

However, as discussed above, Wolf-Klein et al teaches that there is no medical treatment currently available to cure or stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new

technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.). Moreover, the specification of the instant application in p. 3 acknowledges that the delaying and reversing the progression is largely unsuccessful. The specification of the instant application states:

> The management of AD consists of medication-based and non-medication based treatments. Treatments aimed at changing the underlying course of the diseases (delaying or reversing the progression) have so far been largely unsuccessful.

Further, claim 27 recites the intended use of the constructs in treatment for AD, multidrug resistance in cancer cells or prion diseases. For the reasons addressed previously, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 19, 20 and 23-37 stand rejected under 35. U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of supramolecular antigenic constructs wherein the antigenic construct is a SEQ ID NOs:1-6 with a modification such as palmitoylation; however, Applicant is not in possession of any supramolecular antigenic constructs comprising any unspecified amyloid peptides with modification.

The claims broadly encompass any peptide from any amyloid protein in any lengths. The specification does not provide written description for such broad genus peptide encompassed by the claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The guidelines of the Examination of Patent Applications Under the 35 U.S.C. 112 § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e.., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106, column 3).

The antigenic peptide of the instant claims is drawn to any peptide that is obtained from any amyloid protein. The specification of the instant application discloses some peptides (as in claim 25) that are derived from Aβ amyloid. However, the claimed peptide is not limited to Aβ amyloid but encompasses any amyloid proteins. It is noted that amyloid is defined as any complex protein that is deposited in tissues and shares selected laboratory features such as a change in the fluorescence intensity of certain aromatic dyes (Medicine Net definition, 8/8/04, of record) and there are number of other amyloids does not have any structural relationship with Aβ amyloid (wikipedia, 2009, p. 1-6, of record). Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of peptides that are non

Aβ amyloid. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than Aβ amyloid sequences of claim 25.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant's arguments filed on 12/10/09 have been fully considered but they were not persuasive.

Applicant has asserted that the current amendment reciting "construct comprises an antigenic peptide having the amino acid sequence of β amyloid or an active fragment thereof" provides sufficient written description and obviates the rejection.

Contrary to Applicant's assertion, the claimed peptide is not limited to β amyloid or fragments thereof but includes any antigenic polypeptide that encompasses the fragment of β amyloid and other unspecified amino acid sequences in addition to the β amyloid sequence. Note that the term "having" is considered open and allows addition of unspecified amino acid sequences to the either ends of β amyloid fragment. Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of antigenic peptides that comprise any fragments of β amyloid and unspecified amino acids. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than β amyloid sequences of claim 25.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 19, 20 and 23-27 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al. (PNAS, 2002 vol. 99, no. 4, p. 2332-2337, IDS reference, of record) for the reasons set forth in the office action mailed on 8/11/09.

Applicant's arguments filed on 12/10/09 have been fully considered but they were not persuasive.

Applicant has asserted that the Nicolau et al. express serious doubt to the NOBRA mouse model in the treatment of Alzheimer's diseases because the NOBRA model does not provide a blood-brain barrier to cross for the antibodies to reach the pancreatic plaques. Applicant has further asserted that Nicolau et al. fails to provide any action of administering the compound on plaque deposition in the brain or reduce symptoms of AD. Moreover, Applicant has asserted that the prior art does not teach the claimed limitation as currently amended reciting "delaying or reversing the progression of Alzheimer's disease"

Contrary to Applicant's assertion, the claimed method does not recite delaying or reversing the progression of AD via the antibodies removing plaques deposited in the brain. Rather, the claimed method is drawn to delaying or reversing the progression of AD comprising administering the supramolecular construct and does not specify the patient group which the supramolecular construct is being administered to.

Further, Nicolau et al. suggest different mechanisms of destruction of plaques including opsonization of the plaques and the subsequent destruction by microglia macrophages, alteration of the transport and equilibrium of β amyloid between brain and plasma and direct interaction of β amyloid antibodies with the plaque.

Contrary to Applicant's assertion in that Nicolau et al. do not teach delaying and reversing the progression of AD, Fig. 4 (p. 2335) has demonstrated disaggregation of β amyloid fibrils. This indicates the reduction of β amyloid plaques (abstract). Note that the results indicated that the palmitylated β amyloid peptide reconstituted in liposomes-lipid A are highly immunogenic, eliciting "therapeutic" antibody titers within 3 months of the first inoculation and preventing β amyloid plaque formation in young animals or significantly reducing existing plaques in older transgenic mice (abstract, Figs 2-5).

As discussed previously, Nicolau et al. teach administration of antigenic composition comprising a peptide comprising the claimed SEQ ID NO:1 in a reconstituted liposome comprising phospholipids and cholesterol (Fig.1, p. 2333) in PBS (e.g. pharmaceutical carrier).

Further, Nicolau et al. teach that a hydrophobic (e.g. palmitoylic acid) tail is attached to a lysine residue of the peptide (Introduction, p. 2332) and the peptide is derived from Aβ amyloid sequence.
Given that the identical antigenic composition is administered to a group of subject having Aβ plaques (p. 2333, col. 2), the referenced composition inherently delays or reverses the progression of Alzheimer's diseases by enhancing antigenicity.

Even if the claimed method does not recite a particular patient population, the patient population having Aβ plaques cannot be excluded from the study because having Aβ plaques is considered as indication of Alzheimer's disease (p. 2332). Thus, prior art population and the potential population of the claimed method are considered identical. Therefore, the reference teachings anticipate the claimed invention.

10. No claims are allowable.

11. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F,9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Yunsoo Kim
Patent Examiner
Technology Center 1600
March 16, 2010

/Michael Szperka/
Primary Examiner, Art Unit 1644